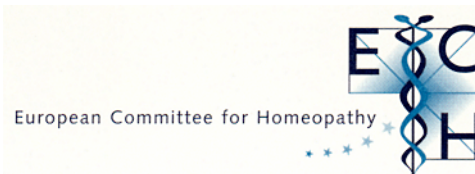


REPORT ON SWISS REPORT ON THE COMPLEMENTARY MEDICINE EVALUATION PROGRAMME (PEK)



Just recently the final report of the Swiss PEK study has been made public. This study was aimed at investigating the efficacy, appropriateness and cost-effectiveness of five CAM therapies, i.e. anthroposophical medicine, homeopathy, neural therapy, herbal medicine (phytotherapy) and Traditional Chinese Medicine, practised by medical doctors. The study took six years and cost 7 million Swiss Francs (€ 4,5 million).

Below the original summary of the PEK report in English can be found (the PEK report itself is written in German and has summaries in German, French, Italian and English). In addition, some considerations as to the review and analysis of homeopathy trials are mentioned.

Original summary of the final report (Schlussbericht)

Background: Following the decision taken by the Federal Department of Home Affairs (DHA) on 9 July 1998, five complementary therapies – anthroposophical medicine, homeopathy, neural therapy, phytotherapy and Traditional Chinese Medicine (more precisely, traditional Chinese herbal therapy) – were included on 1 July 1999 for a limited period (until 30 June 2005) in the list of services covered by the compulsory health insurance scheme (KLV). These services are only eligible for reimbursement if they are provided by physicians who have the relevant proficiency certificates, issued by the Swiss Medical Association (FMH). The decision on whether these complementary methods should be retained within the basic health insurance scheme is dependent on their efficacy, appropriateness and cost-effectiveness being demonstrated. To this end, the Complementary Medicine Evaluation Programme (PEK) was carried out from 1998 to 2005. The aim of the present Final Report is to summarize the design and results of this programme.

Design of the PEK: In a sometimes difficult process – seeking consensus among representatives of complementary therapies and conventional medicine and methodologists – a basic procedure was defined, comprising two parts. In Part 1 (evaluation of the provision of complementary medicine for patients in Switzerland), empirical studies were to be carried out, permitting conclusions as to: (a) how prevalent the five therapies are in Switzerland, (b) which physicians offer these therapies, (c) which patients have recourse to them, (d) what results are achieved with these treatments, and (e) what impact these therapies have on costs. For points b, c, and e, comparisons were made with conventional medicine. On account of methodological and time-related problems, however, point d could not be evaluated. In Part 2 (literature analysis), the literature available internationally on efficacy, appropriateness (here primarily defined in terms of safety and utilization) and cost-effectiveness was to be systematically compiled and reviewed.

Results of the evaluation of the provision of complementary medicine for patients in Switzerland: In 2002, 10.6% of the Swiss population had recourse to at least one of the five complementary therapies, with homeopathy being the individual method most frequently mentioned. Practitioners of complementary medicine can be distinguished from physicians providing conventional healthcare with regard to the nature, location and technical resources of their practice. The patients they treat tend to be younger, female and better educated. These patients tend to have a favourable attitude towards complementary medicine and to exhibit chronic and more severe forms of disease. Technical diagnostic procedures are performed more rarely, and patients' wishes are taken into account more frequently in the choice of treatment. On average, the consultation lasts markedly longer than in conventional care. Patients are more satisfied with the care provided in practices offering complementary medicine. Side effects are reported by markedly fewer patients than with conventional care – with the

exception of phytotherapy.

With complementary medicine, the total annual costs are markedly lower than the average for conventional care. Overall, however, complementary practitioners treat fewer patients, and more frequently younger and female patients. Adjusted for these factors, the total patient-related costs do not differ significantly from those for conventional care. The cost structure is characterized by a greater weighting for consultation costs and a lower weighting for drug costs. The actual increase in costs resulting from the inclusion of the five complementary therapies in Switzerland's basic healthcare provision proved to be markedly lower than expected. On the basis of the statistics produced by the PEK, the question of whether complementary medicine should be regarded as being utilized in addition to or, rather, instead of conventional care cannot be definitively answered.

Results of the literature analysis: The analysis of the literature involved two different projects.

(1) For each of the five complementary therapies, a comprehensive overall evaluation (evaluation report) was prepared. (2) In addition, meta-analyses (systematic reviews including statistical evaluation of aggregated data) of placebo-controlled clinical studies were prepared for homeopathy, phytotherapy and traditional Chinese herbal therapy. As no or only insufficient placebo-controlled studies were available for anthroposophical medicine and neural therapy, meta-analyses were not carried out in these cases. As regards the first project, the assessment of efficacy was favourable in all of the evaluation reports. For phytotherapy and homeopathy in particular, this was based on the evaluation of published systematic reviews and randomized clinical studies. In the case of traditional Chinese herbal therapy, while numerous randomized studies of Chinese origin exist, they are scarcely available in Western countries. For anthroposophical medicine, a very limited number of randomized studies and a larger number of other studies are available. For neural therapy, a very limited number of studies exist, as well as numerous individual case reports. In the view of the evaluation committee, the interpretation of the available evidence on efficacy in the evaluation reports appears to be overly optimistic for all of the methods reviewed, and especially for neural therapy. The safety of all five therapies is favourably assessed, with certain reservations in the case of neural therapy and traditional Chinese herbal therapy. Data concerning utilization are only available for complementary medicine as a whole; for many countries, the uptake is shown to be high and still increasing. With regard to cost-effectiveness, only isolated studies exist, which do not permit any firm conclusions. For anthroposophical medicine and homeopathy, there is evidence that the costs arising are at least offset by savings elsewhere. As regards the second project, in the view of the authors of the meta-analyses, the available placebo-controlled studies on homeopathy do not demonstrate any clear effect over and above placebo. For phytotherapy, in contrast, a positive result is shown, as in the evaluation report, and for traditional Chinese herbal therapy an unequivocal assessment is not possible. Here, too, the validity of the conclusions of the meta-analyses should be regarded as limited from a methodological perspective.

Most important conclusions as to homeopathy

The PEK study is a type of outcome research and uses components of well-established scientific disciplines such as epidemiology, clinical research, psychometry, health economy and healthcare research. It is focused on perceived effectiveness. This study design avoids the problems of other research models that are far from appropriate for an individualized therapeutic system like homeopathy. The basic assumption of this study is that evidence of effectiveness can be found indirectly if the scientifically defined quality of homeopathic care is equal to that of conventional care, provided that the patient population is comparable.

The study even showed that the quality of homeopathic care was superior to that of conventional care. This difference could not be explained by the seriousness of the illnesses, because homeopathic doctors saw even more seriously and chronically ill people. Especially the rate of children was excessively high,

five times higher than in conventional practice (24% versus 4.5%). Children were hardly referred to pediatricians, because the homeopathic doctor was able to provide the necessary care. Quality of life (SF-36 questionnaire) and physical health score were significantly higher, even after correction for age and gender. Also the satisfaction about the patient-doctor relationship scored significantly higher.

The savings are obvious: less high-tech and high-cost procedures, fewer referrals to medical specialists and hospitals, less use of conventional prescription drugs, no costs from serious adverse effects, shorter sick leaves. Costs of homeopathic practice were about 50% of those of conventional practice. If all 269 homeopathic doctors who were involved in the project would practise conventional medicine, the annual costs would increase with 95-100 million Swiss Francs (€ 60-65 million). It was not possible, within the scope of this study, to calculate the savings as a result of the lower referral rate to specialists and hospitals, prevented costs of adverse effects of prescription drugs, fewer sick leave days etc.

It seems that the homeopathic doctors do not provide complementary medicine in the sense of an addition to regular medicine, but in fact another type of primary care.

Some considerations as to the review and analysis of homeopathy trials

The authors of the report emphasise that homeopathy, from its inception, has been based on empirical research and individual medicine selection. Mainstream research studies usually ignore the basic rules of the homeopathy and are usually without any value to actual homeopathic practice. In other words, the external validity is low and therefore there is a high risk of false-negative results. Especially the "gold standard" randomized controlled studies (RCT) forces homeopathy into a straightjacket. The historical evidence, the case reports and 200 years practice on millions of patients: this "soft" evidence can and should not be completely ignored. In spite of these problems it has been possible to show the efficacy and clinical effectiveness of homeopathy in numerous studies set-up according to conventional criteria.

The report includes a review and analysis of homeopathy trials, based on an extensive literature search and predefined quality criteria and including both systematic reviews and individual randomized clinical trials. The comprehensive evaluation section contains the following information: The assessment included 22 systematic reviews, 10 of which covered homeopathy as an entire therapy system (i.e. no limitation in the type of the intervention or illness), 7 of which the effectiveness in individual illnesses, 3 a specific homeopathic medicine and 2 a certain homeopathic medicine in a defined medical condition. 20 of the 22 reviews found at least a trend in favour of homeopathy. In the authors' view 5 of these reviews even show clear evidence for the effectiveness. On the basis of the available reviews the authors classify the 'everyday effectiveness' of homeopathy on a three-stage (probable, questionable, improbable) scale as 'probable'. Since almost all reviews were limited to randomized studies, whose relevance for homeopathic practice was regarded as doubtful, all 29 found and available studies in the indication area of upper respiratory tract infections were analyzed. 17 studies were randomized, 10 not-randomized controlled and one retrospectively; one study was an individual case report. The result was classified as positive in 22 of 29 studies. In 7 of the 14 placebo-controlled studies the homeopathic intervention was significantly superior, a further four studies showed a similar trend. When comparing with conventional therapy a significant superiority of homeopathy was found in one of the 9 studies, and a trend in favour of the homeopathy in another five studies. The methodical quality as well as the relevance to actual practice and the transposition of the results to the Swiss situation were considered to be limited, but this cannot lead to fundamental doubt about the effectiveness of homeopathy in the clinical everyday situation. The authors point out that because most studies have hardly any relevance to actual practice they actually can be considered as 'justification research'. The authors draw the conclusion that there is sufficient evidence for its clinical effectiveness.

Whereas the authors of the overall evaluation report draw the conclusion that there is sufficient evidence for the effectiveness of homeopathy, the authors of the meta-analysis came to a different conclusion. This seems rather odd, because both groups of authors based their conclusions on the same extensive literature search and predefined inclusion criteria, including both systematic reviews and individual randomized clinical trials. In the view of the authors of the meta-analyses, the available placebo-controlled studies on homeopathy do not demonstrate any clear effect over and above placebo.

The meta-analysis was conducted at the Department of Social and Preventive Medicine (ISPM) of the Bern University, under the direction of Prof. Dr Matthias Egger. In their analysis 110 studies on homeopathic interventions were included and matched with 110 studies on conventional interventions. Study features and results were systematically extracted and the methodical quality of the studies was judged by usual criteria. Double-blind studies, in which an adequate randomisation (i.e. appropriate generation of the randomisation sequence and blinding of the randomisation process) was described, were judged as high quality. In all studies the result first was given an odds ratio; an odds ratio = 1 means that no difference between verum and placebo had occurred, a value < 1 a better result under verum and a value > 1 better result under placebo. Then the heterogeneity of the study results (Chi square test and heterogeneity index of I^2) was assessed, i.e. it was checked whether the results of the individual studies – on the assumption that all studies measure the same effect – differ more strongly than would be expected on the basis of coincidental variation. The heterogeneity of the study results can, after a rough categorisation (Higgins et al. Measuring inconsistency in meta-analyses. *BMJ* 2003;327:557-560) be classified as small at a heterogeneity index I^2 of 25%, as medium at an index of 50% and strong at 75%. If a middle or even strong heterogeneity shows up, this means that either the studies measure something different or that disturbing factors are present, which could have falsified the results. In order to examine the causes of the heterogeneity in a better way, different methods were used. Thus it was e.g. examined whether methodically better studies have other results than methodically less good ones. To this aim ‘pooled’ odds ratio of the better studies were divided by that of the less good ones. The resulting ratio is the ‘ratio of odds ratios’ (ROR). A ROR of 1 indicates that there is no difference in estimated treatment effects between these groups of trials whereas a ratio above 1 indicates, for example, that the unpublished trials showed less beneficial treatment effects than the published trials. A ratio below 1 means that in the methodically better studies smaller effects were reported. Above all, however, it was examined whether there was a connection between the size (or more exactly the accuracy) of the study and the size of the difference between verum and placebo. The background of this procedure is the following: If there are e.g. 10 studies, which examine a St. John’s wort preparation in similar patients with light to moderately severe depressions, the results should fluctuate only slightly around the ‘true’ effect. Since coincidence plays the smallest role in the largest studies, these should measure the true effect in a particular reliable way. By contrast, the results of smaller studies fluctuate more widely around the true value, i.e. in some studies the effect is overrated, underestimated in others. If one displays the results of such a group of studies graphically, the well-known picture of a funnel results. If a clearly asymmetrical picture results in such a ‘funnel plot’, it is usually interpreted as a ‘small study bias’, i.e. the smaller studies obtain a distorted picture of the effect. Frequently e.g. smaller negative studies are not published (publication bias) or it comes to an over-estimation of the effect due to methodical errors. There are numerous examples in the literature, which are based on such a small study bias. Therefore in the analyses of the ISPM such funnel plots were used and the extent of observed asymmetry was quantified in a quotient.

The authors of the ISPM study maintain that, if the results of the individual studies are heterogeneous and there is evidence that available larger and/or better studies furnish other results than smaller and/or worse ones, pooling (meta-analysis) of all studies is problematic. Since it is assumed that larger and better studies furnish more reliable results, only this subgroup of studies was used for the main analysis as to the question of effectiveness over placebo.

Additionally it was estimated with the help of statistical methods (meta-regression), how the effect is expected in virtual large studies. The results again were represented as odds ratios, completed with a 95%

confidence interval. If this excludes the value 1, the difference between verum and placebo is statistically significant. The biomedical studies were analysed in the same way. They were used as comparison check, in order to check whether in the conventional interventions similar samples show up as in the complementary procedures.

The methodological quality of homeopathic and conventional studies was mostly similar, although the homeopathic studies tended to have higher quality: 19% of the homeopathic and 8% of the conventional studies were classified as 'higher quality'. In most studies the odds ratios were < 1 , i.e. a (statistically not always significant) better effect from verum. The heterogeneity of the study results were clear in the homeopathic interventions (heterogeneity index I^2 of 65%), in the conventional studies even more pronounced (I^2 of 77%). The funnel plots for both study groups were clearly asymmetrical, i.e. smaller studies show stronger effects. In the methodologically higher quality studies the effects in both groups were clearly smaller (ROR 0.62 and 0.61). When pooling the 8 largest methodologically higher quality homeopathic studies, there was no significant effect beyond placebo (odds ratio 0.88, 95% confidence interval 0.65-1.19). In the 6 largest higher quality conventional studies a significant effect was shown (odds ratio 0.58, 95% confidence interval 0.39-0.85). Also when the effects were estimated in virtually large studies, the homeopathic studies showed no significant effect (odds ratio 0.96, 95% confidence interval 0.73-1.25), but conventional medicine did (odds ratio 0.67, 95% confidence interval 0.48-0.91). The authors conclude that the results support the hypothesis that the clinical effects, in contrast to the effects of conventional medicine, are unspecific placebo or context effects.

The authors admit that the conclusion of the meta-analysis contradicts the evaluation study, although the literature under study is identical. The main reason for this contradiction is that the predominantly positive results of the studies, which were confirmed in the meta-analysis, were interpreted as reliable in the evaluation study, but they were not in the meta-analysis. The authors maintain that for both positions arguments can be found, and that the question which position is more highly estimated, might be strongly influenced by the respective 'prejudices' ('from a conventional scientific point of view homeopathy has no plausible working mechanism') and methodical priorities. A consensus seems to be improbable here. In their conclusion the authors admit that a lack of plausibility cannot be considered as evidence of ineffectiveness. Nor is it a stringent criterion in evidence-based medicine.

The Swiss Association of Homeopathic Doctors (SVHÄ) highly criticizes the report and asserts that this study has serious flaws. In the first place this study includes only RCTs, whereas this research method is less appropriate in more complex therapeutic interventions such as homeopathy. External validity is virtually none. It is fully unclear how many single studies (and which ones) showed a positive or inconclusive/negative result and how these results were assessed. The ISPM study does not disclose which 8 large high-quality homeopathic studies were finally selected and used for their meta-analysis.

In the funnel plot analysis the authors draw a line from the small and medium-sized studies to the few large, but less effective ones. In the case of homeopathy the continuation of this line moves more in the direction of the placebo line than in the case of allopathy. This way the much larger number of positive studies leads to a negative outcome. In fact, the negative result for homeopathy has been produced by a statistical extrapolation from a few large studies.

The SVHÄ maintains that the funnel plot method with its strong emphasis on study size may be justified in research of homogeneous standardised interventions of conventional drug therapy, but is not appropriate in homeopathic studies with their heterogeneity and complex study problems, for the following reasons: 1. The studies comprise a diversity of study models and homeopathic approaches that simply cannot be boxed together 2. The ISPM method would only be correct for verification of similar study models or homogeneous interventions 3. As a rule: the larger the study, the smaller the chance that appropriate homeopathy is examined, which means the smaller the external validity 4. Homeopathic

studies have the risk of false negative results because of their poor validity for actual practice. Within the framework of these distorted forms of homeopathy there are attempts with positive and others with negative results. A negative result only means that the model to prove the effectiveness is not valid. Positive and negative results cannot cancel each other out. Evidence of effectiveness with distorted forms of homeopathy can only serve as an example.

When searching for large studies that have probably been used for the ISPM meta-analysis, the following ones can be found: Attena et al. (1995) who was not able to demonstrate the preventive action of Oscilloccinum in 1595 individuals, Ferley et al. (1987) who found the same result with a homeopathic complex remedy in 1182 individuals. Although in some other large studies positive results were obtained (Ferly et al. in 1989 in 487 individuals, Rottey et al. in 1995 in 501 individuals, Papp et al. in 1998 in 372 and Diefenbach et al. in 1997 in 258 individuals) the larger numbers of the negative studies outweigh the positive outcome of the other ones in the funnel plot method. Another large study of 1,306 school children in India did not demonstrate any effect of Euphrasia C30 in a conjunctivitis epidemic (Mokkapatti et al. 1992), Vickers et al. in 1998 was not able to demonstrate any preventive or therapeutic effect of Arnica D30 in muscle soreness after long-distance running (519 individuals), in contrast to an earlier study by Tveiten.

The SVHÄ in their critique wonder why the clinical picture was always treated with a standard remedy and why it was with that particular one. In which individuals and to what extent does long-distance running lead to symptoms that need any treatment? From a biomedical point of view this kind of studies may be valid, from a homeopathic point of view they are low quality, not representative and unacceptable. This kind of studies force homeopathy into standard designs unrelated to actual practice. It remains unclear if the remedies could have an effect in specific studies. The studies are dubious attempts to demonstrate the effect of high potencies. The only conclusion can be that the study design does not suit homeopathy, not that homeopathy is ineffective (false negative results with poor external validity): absence of evidence does not mean evidence of absence! From a scientific point of view it is impermissible and lax if one wants to prove the ineffectiveness of homeopathy on the basis of studies of that sort, and if one publishes such studies resulting from one-sided statistical thinking without taking the basic homeopathic principles into account. In addition, the question arises whether the statistical extrapolation to eliminate sources of error does not become a source of error itself. In any case: the scientific conclusion that the ISPM draws from an impermissible extrapolation and generalisation of such studies, is enormous! Highly negligent and scientifically untenable.

Another point of concern was that the ISPM did not include any expert from the field of homeopathy. It was not before January 2005 that homeopathic experts were allowed to peruse the meta-analysis. ISPM Director Prof Egger repeatedly has pronounced his conviction that homeopathy cannot be effective because its working mechanism is implausible. It does not seem to be a particularly unbiased position.

Decision of the Swiss authorities

Although homeopathy and other CAM therapies proved to be cost-effective and may save millions of Swiss Francs on the health budget, the Swiss government decided to **exclude** all CAM therapies from the compulsory health insurance scheme as from 30 June 2005, much to the dissatisfaction of the CAM community (since 1999 they were reimbursed under the compulsory health insurance scheme for the purpose of the PEK study). The reason: there is no scientific evidence for the effectiveness of homeopathy. Only optional health insurance will cover CAM expenditures.

The Swiss authorities – both the government and the National Health Office (BAG) – initially tried to sweep the results of the PEK study under the carpet. A conference scheduled for April 2005 to present and discuss the results of the PEK study had to be cancelled because the National Health Office

suppressed the publication of the study data. Some collaborators were even coerced into deleting all PEK related data from their computers. A final meeting of the international Review Board of 6 professors from Switzerland, Germany, Denmark and the UK – responsible for the scientific quality of the PEK study – to be held in June 2005 for a final assessment of the project, was cancelled. The recommendation in the final draft that homeopathy, anthroposophical medicine and herbal medicine should stay in the compulsory health insurance scheme was deleted in the final publication. Later on the government allowed some reports to be put onto the BAG website and the data files to be available for perusal at the BAG office in Bern.

Unsurprisingly, the medical establishment was far from pleased with the results of the PEK study. Already at the end of 2004 at a conference of the Swiss Academy of Medical Science some professors of the medical university faculties agreed to do anything possible to prevent CAM from remaining available in the compulsory health insurance scheme (they would even “throw grenades”).

Obviously, the CAM doctors do not take it lying down. All CAM doctors associations have now submitted an official request for inclusion of CAM in the compulsory health insurance scheme. The report by the SVHÄ concerning homeopathy, can be found at http://www.dzvhae.com/portal/pics/abschnitte/030605064159_antrag_svha.pdf

An initiative of the general public called “Yes to Complementary Medicine” has already been supported by 145,000 signatures. A survey of March 2005 revealed that 87% of the Swiss population wants CAM to remain reimbursed under the compulsory health insurance scheme and that 31% has seen a CAM doctor at least once in the past year. A member of the Swiss parliament has questioned the government about the issue (to be continued.....).

P.S.

The report on the PEK study (in German) can be downloaded at:

http://www.bag.admin.ch/kv/forschung/f/2005/Schlussbericht_PEK.pdf

The statistical analysis of CAM utilization in Switzerland (also in German) can be found at:

<http://www.bag.admin.ch/kv/forschung/d/2005/Gesundheitsbefragung-KM.pdf>

At the homepage of the Swiss Homeopathic Doctors Association (<http://www.svha.ch>) several interesting articles can be found about the way the Swiss authorities (the government and the National Health Office) and the medical establishment have dealt with the results of the PEK study (most of them in German, some in French).

Report by

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